

Claims

1. Use of at least one compound of the following general formula:

<graphic>

wherein R1 is selected from a group consisting of: H, OH, SH, F, Cl, Br, I, NH₂, N(CH₃)₂, N(C₂H₅)₂, N(C₃H₇)₂; and NH-acyl, wherein the acyl radical contains 1 to 32 carbon atoms, particularly CH₃O, preferably 9 to 32, and more preferably 9 to 20 carbon atoms;

wherein R2 is selected from a group consisting of: H, OH, SH, NH₂, F, Cl, Br, I, O, and S;

wherein R3 is selected from a group consisting of: H, CH₃, and C₂H₅;

wherein R4 and R6 are selected independently from a group consisting of: H, OH, SH, NH₂, F, Cl, Br, I, acetyl, and OX where X is a C1 to C32 acyl radical, particularly a C9 to C32 acyl radical, and preferably a C9 to C20 acyl radical;

wherein R5 is selected from a group consisting of: phenyl, CH₃, C₂H₅, C₃H₇, butyl, isobutyl, and t-butyl;

BEST AVAILABLE COPY

wherein R7 and R8 are selected independently from a group consisting of: H, OH, SH, NH₂, F, Cl, Br, I, CH₃, COOH, CHO, and COOR₉, wherein R₉ is CH₃, C₂H₅, C₃H₇, or butyl;

wherein R₁₀ is selected from a group consisting of: H, CH₃, and C₂H₅, and -- represents an optional double bond; as well as

the pharmaceutically acceptable salts thereof;

for production of a medication to enhance protein tolerance for the treatment of diseases due to amino acid metabolic disorders.

2. Use according to Claim 1 wherein the compound is selected from the group consisting of: 5,6,7,8-tetrahydrobiopterin, sapropterin, particularly the hydrochloride or sulfate thereof, and a compound of the following structure:

<graphic>

(-)-(1'R,2'S,6R)-2-amino-6-(1',2'-dihydroxypropyl)-5,6,7,8-tetrahydro-4(3H)-pteridinone.

Particularly the dihydrochloride thereof, and/or

2-N-stearoyl-1',2'-di-O-acetyl-5,6,7,8-tetrahydrobiopterin; and/or

2-N-decanoyl-1',2'-di-O-acetyl-5,6,7,8-tetrahydrobiopterin; and/or
2-N-palmitoyl-1',2'-di-O-acetyl-5,6,7,8-tetrahydrobiopterin; and/or
2-N-linoleoyl-1',2'-di-O-acetyl-5,6,7,8-tetrahydrobiopterin.

3. Use according to Claim 1 or 2 wherein the hydrochloride or sulfate is used as the salt.
4. Use according to one of Claims 1 through 3 wherein the amino acid metabolic disorders include conditions with elevated phenylalanine or decreased tyrosine in bodily fluids, tissues or cells, particularly conditions with reduced phenylalanine hydroxylase activity, particularly conditions due to decreased cellular availability of catecholamines, particularly orthostatic hypotension (Shy-Drager syndrome), and muscular dystonia; as well as neurotransmitter disorders, particularly schizophrenia; phenylketonuria, particularly mild phenylketonuria, and classic phenylketonuria; and pigment disorders of the skin, particularly vitiligo.
5. Use according to one of Claims 1 through 4 wherein a hydrochloride is used as the pharmaceutically acceptable salt.
6. Use of at least one compound of the following general formula as a chaperone:

<graphic>

wherein R1 is selected from a group consisting of: H, OH, SH, F, Cl, Br, I, NH₂, N(CH₃)₂, N(C₂H₅)₂, N(C₃H₇)₂; and NH-acyl, wherein the acyl radical contains 1 to 32 carbon atoms, particularly CH₃O, preferably 9 to 32, and more preferably 9 to 20 carbon atoms;

wherein R2 is selected from a group consisting of: H, OH, SH, NH₂, F, Cl, Br, I, O, and S;

wherein R3 is selected from a group consisting of: H, CH₃, and C₂H₅;

wherein R4 and R6 are selected independently from a group consisting of: H, OH, SH, NH₂, F, Cl, Br, I, acetyl, and OX where X is a C1 to C32 acyl radical, particularly a C9 to C32 acyl radical, and preferably a C9 to C20 acyl radical;

wherein R5 is selected from a group consisting of: phenyl, CH₃, C₂H₅, C₃H₇, butyl, isobutyl, and t-butyl;

wherein R7 and R8 are selected independently from a group consisting of: H, OH, SH, NH₂, F, Cl, Br, I, CH₃, COOH, CHO, and COOR₉, wherein R₉ is CH₃, C₂H₅, C₃H₇, or butyl;

wherein R10 is selected from a group consisting of: H, CH₃, and C₂H₅, and – represents an optional double bond; as well as

the pharmaceutically acceptable salts thereof.

7. Use according to Claim 6 wherein the compound is selected from the group composed of: 5,6,7,8-tetrahydrobiopterin, sapropterin, particularly the hydrochloride thereof, and a compound of the following structure:

<graphic>

(-)-(1'R,2'S,6R)-2-amino-6-(1',2'-dihydroxypropyl)-5,6,7,8-tetrahydro-4(3H)-pteridinone.

Particularly the dihydrochloride or sulfate thereof, and/or
2-N-stearoyl-1',2'-di-O-acetyl-5,6,7,8-tetrahydrobiopterin; and/or
2-N-decanoyl-1',2'-di-O-acetyl-5,6,7,8-tetrahydrobiopterin; and/or
2-N-palmitoyl-1',2'-di-O-acetyl-5,6,7,8-tetrahydrobiopterin; and/or
2-N-linoleoyl-1',2'-di-O-acetyl-5,6,7,8-tetrahydrobiopterin.

8. Use according to Claim 6 or 7 for improvement of protein misfolding, particularly in the case of structural abnormalities in enzymes that require tetrahydrobiopterin as a cofactor.

9. Use according to one of Claims 6 through 8 wherein the enzymes are selected from: phenylalanine hydroxylase, tyrosine hydroxylase, tryptophan hydroxylase, or NO synthase.
10. Use according to one of Claims 6 through 9 wherein the chaperone is used as a neurotransmitter and/or messenger enhancer, particularly in conditions with elevated phenylalanine or decreased tyrosine, serotonin or dopamine in bodily fluids, tissues or cells, particularly in conditions with decreased phenylalanine hydroxylase, tyrosine hydroxylase, tryptophan hydroxylase and NO synthase activity.
11. Use of at least one compound of the following general formula as a neurotransmitter or as a messenger enhancer, particularly for catecholamines and/or serotonin and/or dopamine and or nitric oxide (NO):

<graphic>

wherein R1 is selected from a group consisting of: H, OH, SH, F, Cl, Br, I, NH₂, N(CH₃)₂, N(C₂H₅)₂, N(C₃H₇)₂; and NH-acyl, wherein the acyl radical contains 1 to 32 carbon atoms, particularly CH₃O, preferably 9 to 32, and more preferably 9 to 20 carbon atoms;

wherein R2 is selected from a group consisting of: H, OH, SH, NH₂, F, Cl, Br, I, O, and S;

wherein R3 is selected from a group consisting of: H, CH₃, and C₂H₅;

wherein R4 and R6 are selected independently from a group consisting of: H, OH, SH, NH₂, F, Cl, Br, I, acetyl, and OX where X is a C1 to C32 acyl radical, particularly a C9 to C32 acyl radical, and preferably a C9 to C20 acyl radical;

wherein R5 is selected from a group consisting of: phenyl, CH₃, C₂H₅, C₃H₇, butyl, isobutyl, and t-butyl;

wherein R7 and R8 are selected independently from a group consisting of: H, OH, SH, NH₂, F, Cl, Br, I, CH₃, COOH, CHO, and COOR₉, wherein R₉ is CH₃, C₂H₅, C₃H₇, or butyl;

wherein R10 is selected from a group consisting of: H, CH₃, and C₂H₅, and -- represents an optional double bond; as well as the pharmaceutically acceptable salts thereof.

12. Use according to Claim 11 wherein the compound is selected from the group consisting of: 5,6,7,8-tetrahydrobiopterin, sapropterin, particularly the hydrochloride thereof, and a compound of the following structure:

<graphic>

(-)-(1'R,2'S,6R)-2-amino-6-(1',2'-dihydroxypropyl)-5,6,7,8-tetrahydro-4(3H)-pteridinone.

Particularly the dihydrochloride or sulfate thereof, and/or

2-N-stearoyl-1',2'-di-O-acetyl-5,6,7,8-tetrahydrobiopterin; and/or

2-N-decanoyl-1',2'-di-O-acetyl-5,6,7,8-tetrahydrobiopterin; and/or

2-N-palmitoyl-1',2'-di-O-acetyl-5,6,7,8-tetrahydrobiopterin; and/or

2-N-linoleoyl-1',2'-di-O-acetyl-5,6,7,8-tetrahydrobiopterin.

13. Composition containing at least one compound of the following general formula:

<graphic>

wherein R¹ is selected from a group consisting of: H, OH, SH, F, Cl, Br, I, NH₂, N(CH₃)₂, N(C₂H₅)₂, N(C₃H₇)₂; and NH-acyl, wherein the acyl radical

contains 1 to 32 carbon atoms, particularly CH_3O , preferably 9 to 32, and more preferably 9 to 20 carbon atoms;

wherein R_2 is selected from a group consisting of: H, OH, SH, NH_2 , F, Cl, Br, I, O, and S;

wherein R_3 is selected from a group consisting of: H, CH_3 , and C_2H_5 ;

wherein R_4 and R_6 are selected independently from a group consisting of: H, OH, SH, NH_2 , F, Cl, Br, I, acetyl, and OX where X is a C1 to C32 acyl radical, particularly a C9 to C32 acyl radical, and preferably a C9 to C20 acyl radical;

wherein R_5 is selected from a group consisting of: phenyl, CH_3 , C_2H_5 , C_3H_7 , butyl, isobutyl, and t-butyl;

wherein R_7 and R_8 are selected independently from a group consisting of: H, OH, SH, NH_2 , F, Cl, Br, I, CH_3 , COOH, CHO, and COOR₉, wherein R_9 is CH_3 , C_2H_5 , C_3H_7 , or butyl;

wherein R_{10} is selected from a group consisting of: H, CH_3 , and C_2H_5 , and -- represents an optional double bond; as well as

the pharmaceutically acceptable salts thereof; as well as

containing at least one amino acid selected from the group consisting of the essential amino acids: isoleucine, leucine, lysine, methionine, threonine, tryptophan, valine, and histidine; as well as the non-essential amino acids, particularly alanine, arginine, asparaginic acid, asparagine, cysteine, especially acetylcysteine, glutamic acid, glutamine, glycine, proline, serine and tyrosine.

14. Composition according to Claim 13 wherein it contains essential amino acids selected from the group consisting of: isoleucine, leucine, lysine, methionine, threonine, tryptophan, valine, and histidine and at least one of the amino acids alanine, arginine, asparaginic acid, asparagine, cysteine, especially acetylcysteine, glutamic acid, glutamine, glycine, proline, serine and tyrosine.
15. Composition according to Claim 13 or 14 wherein it contains additional carbohydrates, particularly glucose, and/or vitamins.
16. Composition according to one of Claims 13 through 15 wherein it is formulated as a preparation to be administered orally or intravenously.
17. Composition according to Claim 16 wherein the preparation is formulated as a powder, tablet, capsule, coated tablet, drops or for topical use, particularly salves; as well as a solution for intravenous administration.
18. Composition according to Claims 14 through 17 wherein it is formed as a pharmaceutically composition, with the usual galenic pharmaceutical adjuvants, if necessary.
19. Composition according to one of Claims 13 through 18 wherein it is formed as a dietary composition, with the adjuvants usual in foodstuffs technology, particularly emulsifiers, preferably lecithin or choline, if necessary.

20. Composition according to one of Claims 13 through 19 wherein it contains additional minerals and/or electrolytes selected from: mineral salts; saline salts; sea salts; trace elements, particularly selenium, manganese, copper, zinc, molybdenum, iodine, chromium; alkali ions, particularly lithium, sodium and potassium; earth alkali ions, particularly magnesium and calcium; and iron.
21. Composition according to one of Claims 13 through 20 wherein it contains additional phenylalanine.
22. Composition according to one of Claims 13 through 21 wherein it contains additional L-carnitine.
23. Composition according to one of Claims 13 through 22 wherein it contains additional myoinositol and choline.
24. Compositions according to one of Claims 13 through 23 wherein it contains antioxidants, particularly Vitamin C.
25. Composition according to one of Claims 13 through 24 wherein the compound is selected from the group consisting of 5,6,7,8-

tetrahydrobiopterin, sapropterin, particularly the hydrochloride thereof, and a compound of the following structure:

<graphic>

(-)-(1'R,2'S,6R)-2-amino-6-(1',2'-dihydroxypropyl)-5,6,7,8-tetrahydro-4(3H)-pteridinone.

Particularly the dihydrochloride or sulfate thereof, and/or

2-N-stearoyl-1',2'-di-O-acetyl-5,6,7,8-tetrahydrobiopterin; and/or

2-N-decanoyl-1',2'-di-O-acetyl-5,6,7,8-tetrahydrobiopterin; and/or

2-N-palmitoyl-1',2'-di-O-acetyl-5,6,7,8-tetrahydrobiopterin; and/or

2-N-linoleoyl-1',2'-di-O-acetyl-5,6,7,8-tetrahydrobiopterin.

26. Use of at least one compound of the following general formula:

<graphic>

wherein R1 is selected from a group consisting of: H, OH, SH, F, Cl, Br, I, NH₂, N(CH₃)₂, N(C₂H₅)₂, N(C₃H₇)₂; and NH-acyl, wherein the acyl radical contains 1 to 32 carbon atoms, particularly CH₃O, preferably 9 to 32, and more preferably 9 to 20 carbon atoms;

wherein R2 is selected from a group consisting of: H, OH, SH, NH₂, F, Cl, Br, I, O, and S;

wherein R3 is selected from a group consisting of: H, CH₃, and C₂H₅;

wherein R4 and R6 are selected independently from a group consisting of: H, OH, SH, NH₂, F, Cl, Br, I, acetyl, and OX where X is a C1 to C32 acyl radical, particularly a C9 to C32 acyl radical, and preferably a C9 to C20 acyl radical;

wherein R5 is selected from a group consisting of: phenyl, CH₃, C₂H₅, C₃H₇, butyl, isobutyl, and t-butyl;

wherein R7 and R8 are selected independently from a group consisting of: H, OH, SH, NH₂, F, Cl, Br, I, CH₃, COOH, CHO, and COOR₉, wherein R₉ is CH₃, C₂H₅, C₃H₇, or butyl;

wherein R10 is selected from a group consisting of: H, CH₃, and C₂H₅, and -- represents an optional double bond; as well as as a dietary supplement.

27. Use according to Claim 26 wherein the compound is selected from the group consisting of: 5,6,7,8-tetrahydrobiopterin, sapropterin, particularly the hydrochloride thereof, and a compound of the following structure:

<graphic>

(-)-(1'R,2'S,6R)-2-amino-6-(1',2'-dihydroxypropyl)-5,6,7,8-tetrahydro-4(3H)-pteridinone.

Particularly the dihydrochloride or sulfate thereof, and/or

2-N-stearoyl-1',2'-di-O-acetyl-5,6,7,8-tetrahydrobiopterin; and/or

2-N-decanoyl-1',2'-di-O-acetyl-5,6,7,8-tetrahydrobiopterin; and/or

2-N-palmitoyl-1',2'-di-O-acetyl-5,6,7,8-tetrahydrobiopterin; and/or

2-N-linoleoyl-1',2'-di-O-acetyl-5,6,7,8-tetrahydrobiopterin.

28. Special food based on mixtures of essentially phenylalanine-free mixtures, wherein it contains at least one compound of the following general formula:

<graphic>

wherein R1 is selected from a group consisting of: H, OH, SH, F, Cl, Br, I, NH₂, N(CH₃)₂, N(C₂H₅)₂, N(C₃H₇)₂; and NH-acyl, wherein the acyl radical contains 1 to 32 carbon atoms, particularly CH₃O, preferably 9 to 32, and more preferably 9 to 20 carbon atoms;

wherein R2 is selected from a group consisting of: H, OH, SH, NH₂, F, Cl, Br, I, O, and S;

wherein R3 is selected from a group consisting of: H, CH₃, and C₂H₅;

wherein R4 and R6 are selected independently from a group consisting of: H, OH, SH, NH₂, F, Cl, Br, I, acetyl, and OX where X is a C1 to C32 acyl radical, particularly a C9 to C32 acyl radical, and preferably a C9 to C20 acyl radical;

wherein R5 is selected from a group consisting of: phenyl, CH₃, C₂H₅, C₃H₇, butyl, isobutyl, and t-butyl;

wherein R7 and R8 are selected independently from a group consisting of: H, OH, SH, NH₂, F, Cl, Br, I, CH₃, COOH, CHO, and COOR₉, wherein R₉ is CH₃, C₂H₅, C₃H₇, or butyl;

wherein R10 is selected from a group consisting of: H, CH₃, and C₂H₅, and -- represents an optional double bond; as well as

the salts thereof acceptable in foodstuffs technology.

29. Special food according to Claim 28 wherein it contains at least one compound selected from the group 5,6,7,8-tetrahydrobiopterin, sapropterin, particularly the hydrochloride thereof, and a compound of the following structure:

<graphic>

(-)-(1'R,2'S,6R)-2-amino-6-(1',2'-dihydroxypropyl)-5,6,7,8-tetrahydro-4(3H)-pteridinone.

Particularly the dihydrochloride or sulfate thereof, and/or

2-N-stearoyl-1',2'-di-O-acetyl-5,6,7,8-tetrahydrobiopterin; and/or

2-N-decanoyl-1',2'-di-O-acetyl-5,6,7,8-tetrahydrobiopterin; and/or

2-N-palmitoyl-1',2'-di-O-acetyl-5,6,7,8-tetrahydrobiopterin; and/or

2-N-linoleoyl-1',2'-di-O-acetyl-5,6,7,8-tetrahydrobiopterin.

30. Special food according to Claim 28 or 29 wherein it contains additional carbohydrates, particularly glucose, maltodextrin, starches and/or fats, such as fish oil, particularly salmon oil, herring oil, mackerel oil, or tuna fish oil.
31. Special food according to one of Claims 28 through 30 wherein it is hypoallergenic and/or essentially gluten-free.
32. Special food according to one of Claims 28 through 31 wherein it is an infant formula.

33. Special food according to one of Claims 28 through 32 wherein it is presented as a powder, particularly a freeze-dried powder.
34. Special food according to one of Claims 28 through 33 wherein it contains additional fatty acid supplements, particularly unsaturated fatty acids, preferably omega 3 fatty acids, especially alpha-linolenic acid, docosahexaenoic acid, eicosapentaenoic acid, or omega 6 fatty acids, in particular arachidonic acid, linoleic acid, or lineolenic acid; or oleic acid.
35. Special food according to one of Claims 28 through 34 wherein it contains fish oil additives, particularly salmon, herring, mackerel or tuna fish oil.
36. Special food according to one of Claims 28 through 35 wherein it can be used as a milk substitute, particularly for nursing infants.
37. Special food according to Claim 36 wherein the milk substitute has a fat content, present particularly as 90% triglycerides and 10% mono- and diglycerides.
38. Special food according to Claim 37 wherein the fat component includes plants oils, particularly safflower oils and/or soybean oil and/or coco oil.

39. Special food according to one of Claims 28 through 38 wherein the milk substitute is formed as a milk drink mix, particularly a fruit-flavored or chocolate drink mix.
40. Special low-phenylalanine foodstuff containing a low-protein basic food as well as at least one compound of the following general formula:

<graphic>

wherein R1 is selected from a group consisting of: H, OH, SH, F, Cl, Br, I, NH₂, N(CH₃)₂, N(C₂H₅)₂, N(C₃H₇)₂, and NH-acyl, wherein the acyl radical contains 1 to 32 carbon atoms, particularly CH₃O, preferably 9 to 32, and more preferably 9 to 20 carbon atoms;

wherein R2 is selected from a group consisting of: H, OH, SH, NH₂, F, Cl, Br, I, O, and S;

wherein R3 is selected from a group consisting of: H, CH₃, and C₂H₅;

wherein R4 and R6 are selected independently from a group consisting of: H, OH, SH, NH₂, F, Cl, Br, I, acetyl, and OX where X is a C1 to C32 acyl radical,

particularly a C9 to C32 acyl radical, and preferably a C9 to C20 acyl radical;
wherein R5 is selected from a group consisting of: phenyl, CH₃, C₂H₅, C₃H₇, butyl, isobutyl, and t-butyl;
wherein R7 and R8 are selected independently from a group consisting of: H, OH, SH, NH₂, F, Cl, Br, I, CH₃, COOH, CHO, and COOR₉, wherein R₉ is CH₃, C₂H₅, C₃H₇, or butyl;
wherein R10 is selected from a group consisting of: H, CH₃, and C₂H₅, and -- represents an optional double bond; as well as
the salts thereof acceptable in foodstuffs technology.

41. Special low-phenylalanine foodstuff according to Claim 40 wherein it contains at least one compound selected from the group consisting of: 5,6,7,8-tetrahydrobiopterin, sapropterin, particularly the hydrochloride thereof, as well as a compound of the following structure:

<graphic>

(-)-(1'R,2'S,6R)-2-amino-6-(1',2'-dihydroxypropyl)-5,6,7,8-tetrahydro-4(3H)-pteridinone.

Particularly the dihydrochloride or sulfate thereof, and/or

2-N-stearoyl-1',2'-di-O-acetyl-5,6,7,8-tetrahydrobiopterin; and/or

2-N-decanoyl-1',2'-di-O-acetyl-5,6,7,8-tetrahydrobiopterin; and/or

2-N-palmitoyl-1',2'-di-O-acetyl-5,6,7,8-tetrahydrobiopterin; and/or
2-N-linoleoyl-1',2'-di-O-acetyl-5,6,7,8-tetrahydrobiopterin.

42. Special low-phenylalanine foodstuff according to Claim 40 or 41 wherein it is selected from: convenience foods; pasta, particularly noodles; baked goods, particularly bread, cakes, and cookies; sweets, particularly chocolate, hard candies, and ice creams; and drinks, particularly milk substitutes in the form of drink mixes, particularly fruit-flavored or chocolate drink mixes; and beer.
43. Diagnostic tool for the diagnosis of tetrahydrobiopterin sensitivity in amino acid metabolic diseases. Containing at least one compound of the following general formula:

<graphic>

wherein R1 is selected from a group consisting of: H, OH, SH, F, Cl, Br, I, NH₂, N(CH₃)₂, N(C₂H₅)₂, N(C₃H₇)₂; and NH-acyl, wherein the acyl radical contains 1 to 32 carbon atoms, particularly CH₃O, preferably 9 to 32, and more preferably 9 to 20 carbon atoms;

wherein R2 is selected from a group consisting of: H, OH, SH, NH₂, F, Cl, Br, I, O, and S;
wherein R3 is selected from a group consisting of: H, CH₃, and C₂H₅;
wherein R4 and R6 are selected independently from a group consisting of: H, OH, SH, NH₂, F, Cl, Br, I, acetyl, and OX where X is a C1 to C32 acyl radical, particularly a C9 to C32 acyl radical, and preferably a C9 to C20 acyl radical;
wherein R5 is selected from a group consisting of: phenyl, CH₃, C₂H₅, C₃H₇, butyl, isobutyl, and t-butyl;
wherein R7 and R8 are selected independently from a group consisting of: H, OH, SH, NH₂, F, Cl, Br, I, CH₃, COOH, CHO, and COOR₉, wherein R₉ is CH₃, C₂H₅, C₃H₇, or butyl;
wherein R10 is selected from a group consisting of: H, CH₃, and C₂H₅, and -- represents an optional double bond;
particularly 5,6,7,8-tetrahydrobiopterin; as well as the pharmaceutically acceptable salts thereof.

44. Use according to Claim 10 wherein the conditions include: phenylketonuria, particularly mild phenylketonuria, and classic phenylketonuria; pigment disorders of the skin, particularly vitiligo; as well as conditions caused by decreased cellular availability of catecholamines, particularly orthostatic hypotension (Shy-Drager syndrome) and muscular dystonia; as well as neurotransmitter disorders, particularly schizophrenia; conditions caused by reduced cellular availability of dopamine or serotonin as a result of tyrosine hydroxylase or tryptophan hydroxylase deficiencies, particularly Parkinson's disease, depressive disorders

and dystonic movement disorders, conditions with reduced NO synthase activity, particularly endothelial dysfunctions, and deficient defense against infections.

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record.**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ **BLACK BORDERS**
- ☐ **IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- ☐ **FADED TEXT OR DRAWING**
- ☐ **BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- ☐ **SKEWED/SLANTED IMAGES**
- ☐ **COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- ☐ **GRAY SCALE DOCUMENTS**
- ☒ **LINES OR MARKS ON ORIGINAL DOCUMENT**
- ☐ **REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- ☐ **OTHER: _____**

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.